SV40 in human tumors: an update NIH 2004

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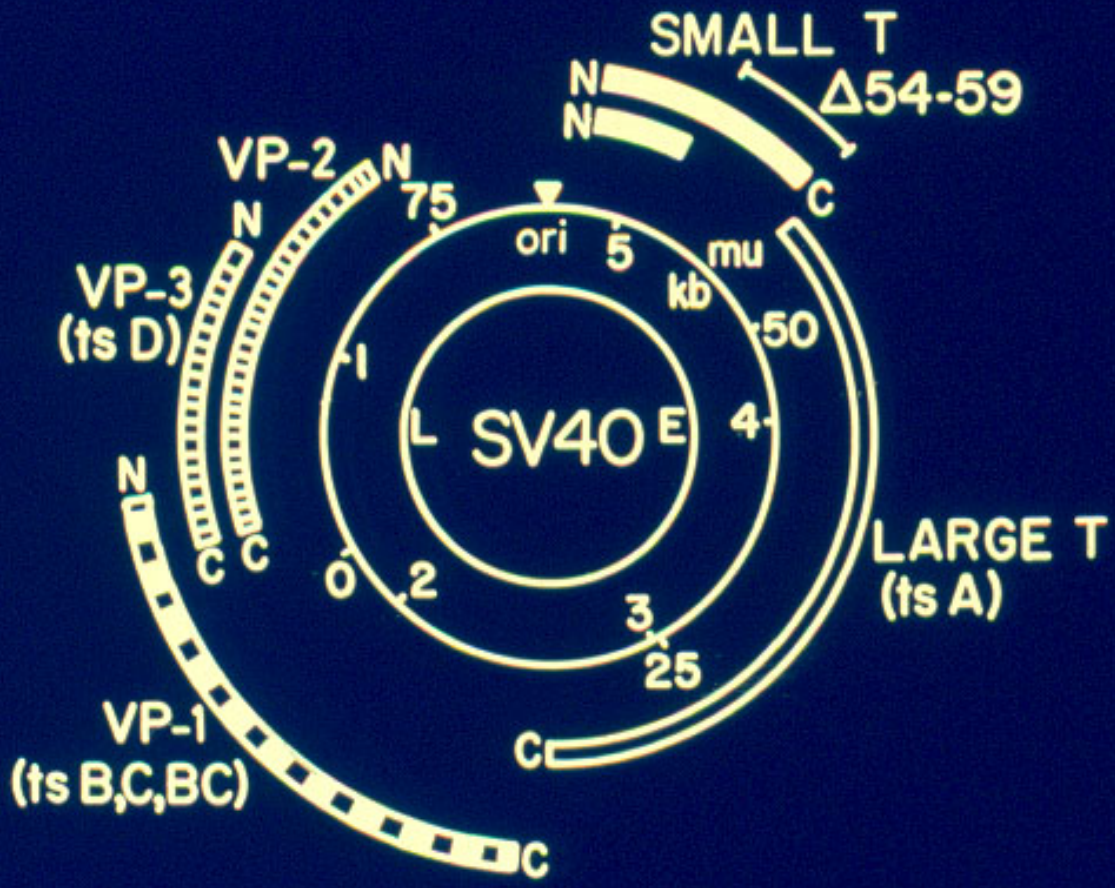
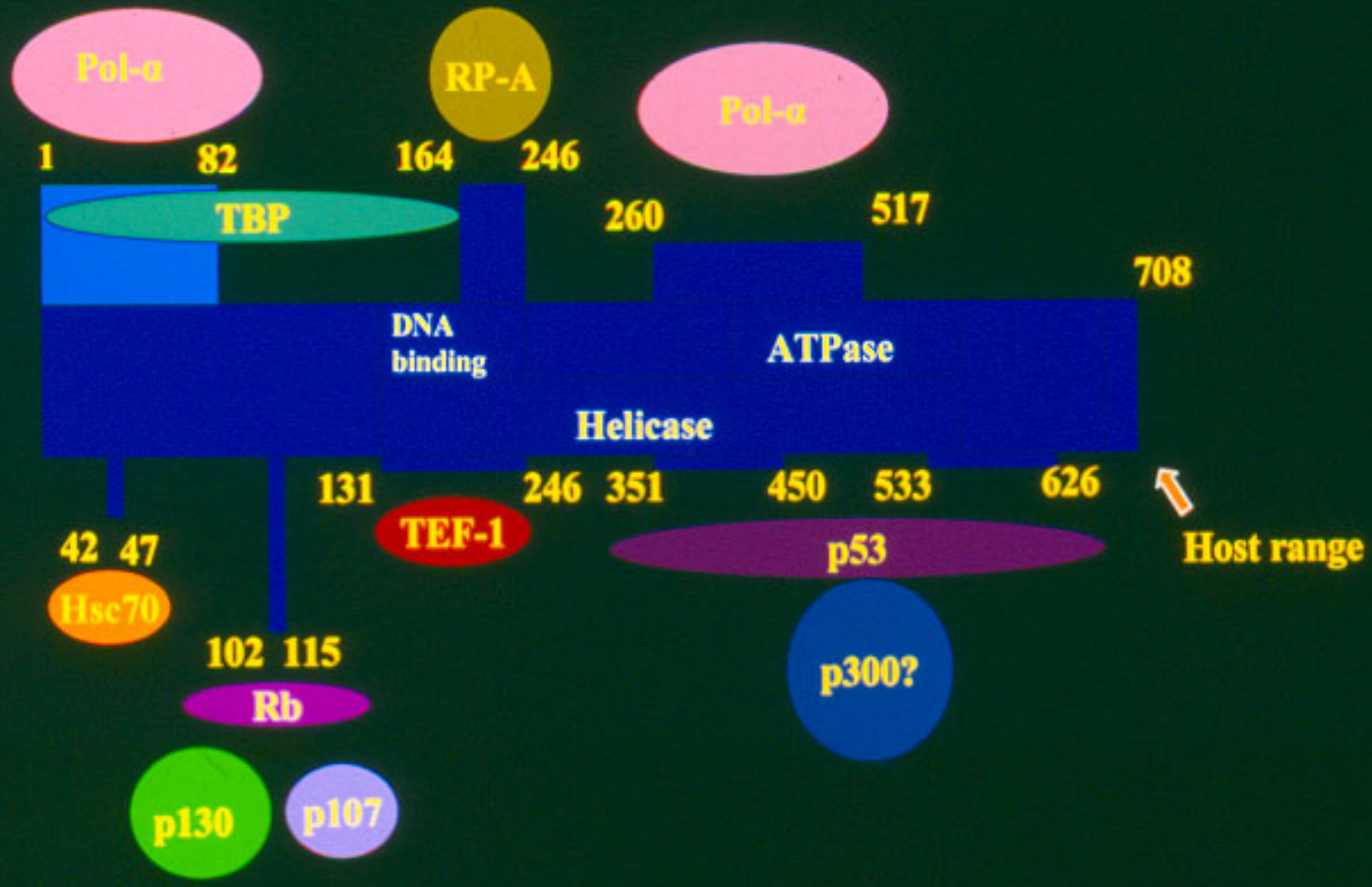
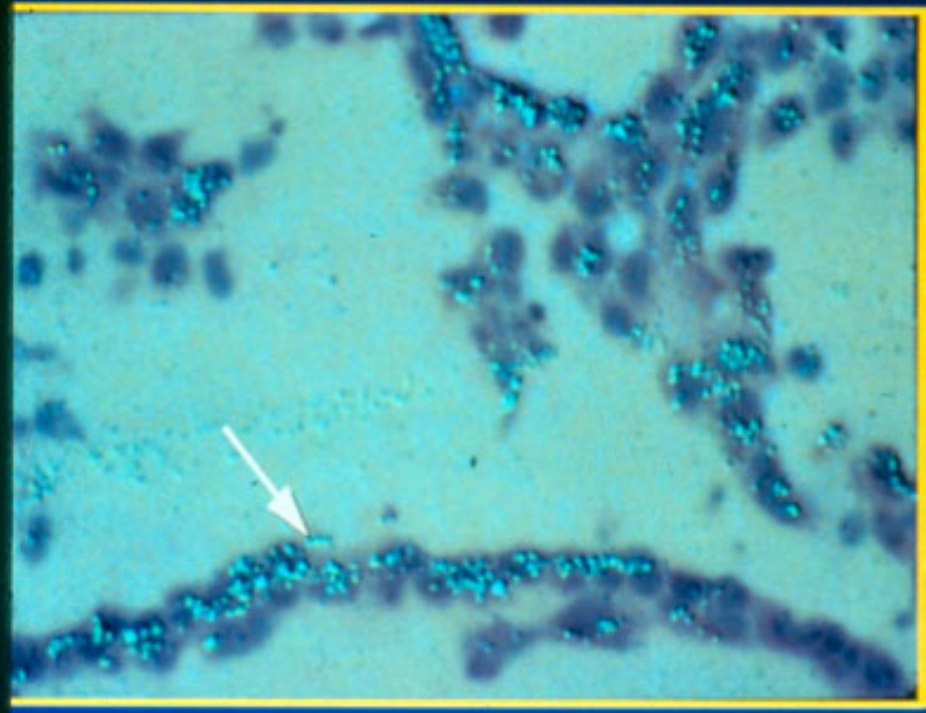
CIRCULAR GENOMIC MAP OF SV40

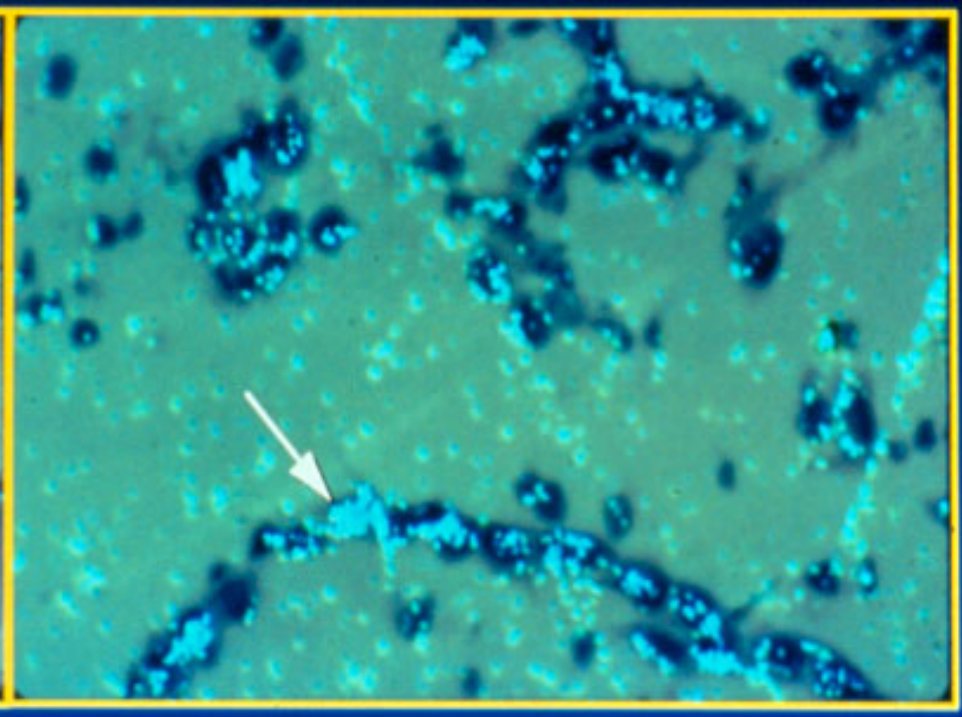


T antigen domains



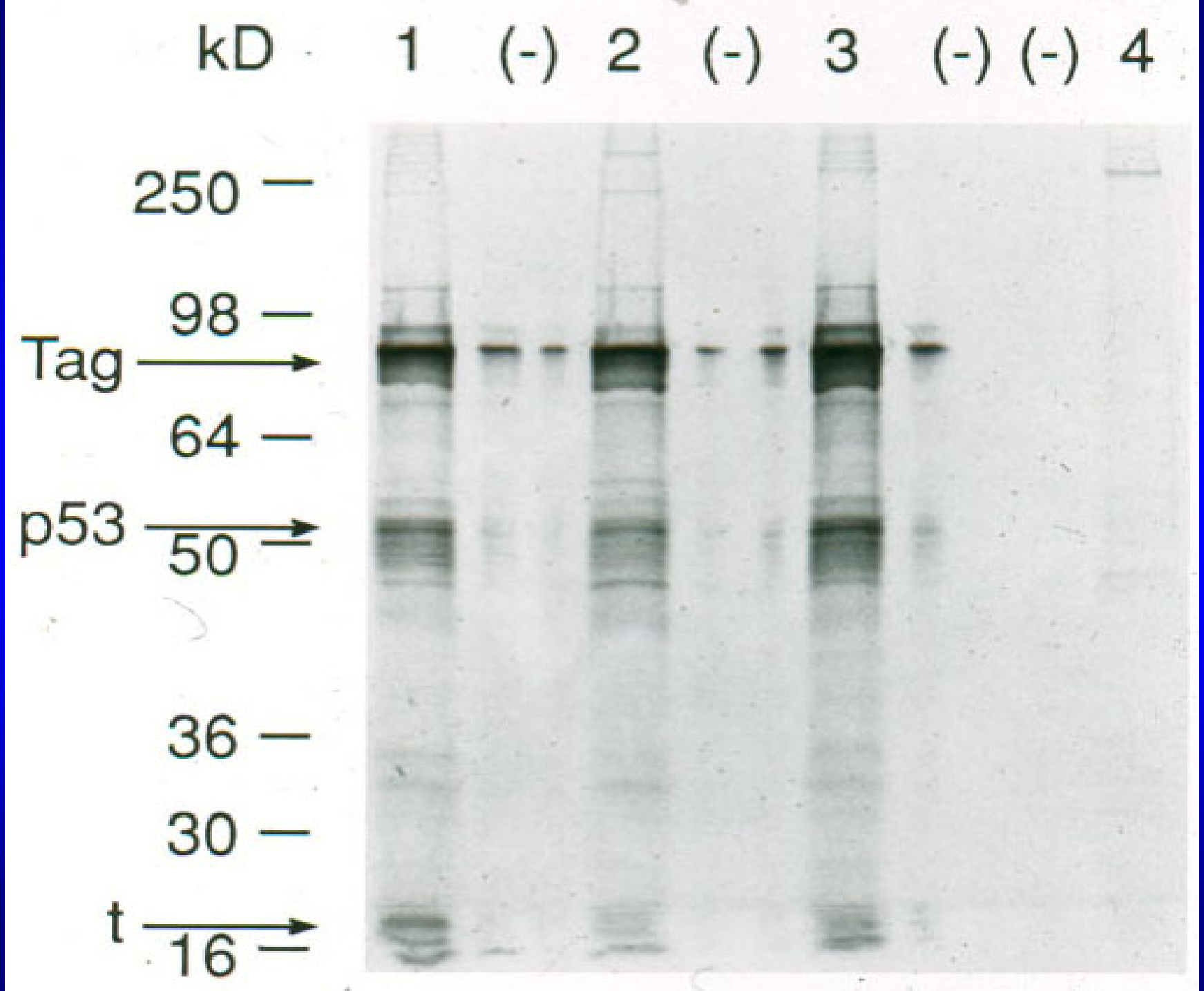
IN SITU





Tag

p53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1
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250
98
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64
p53
50
36
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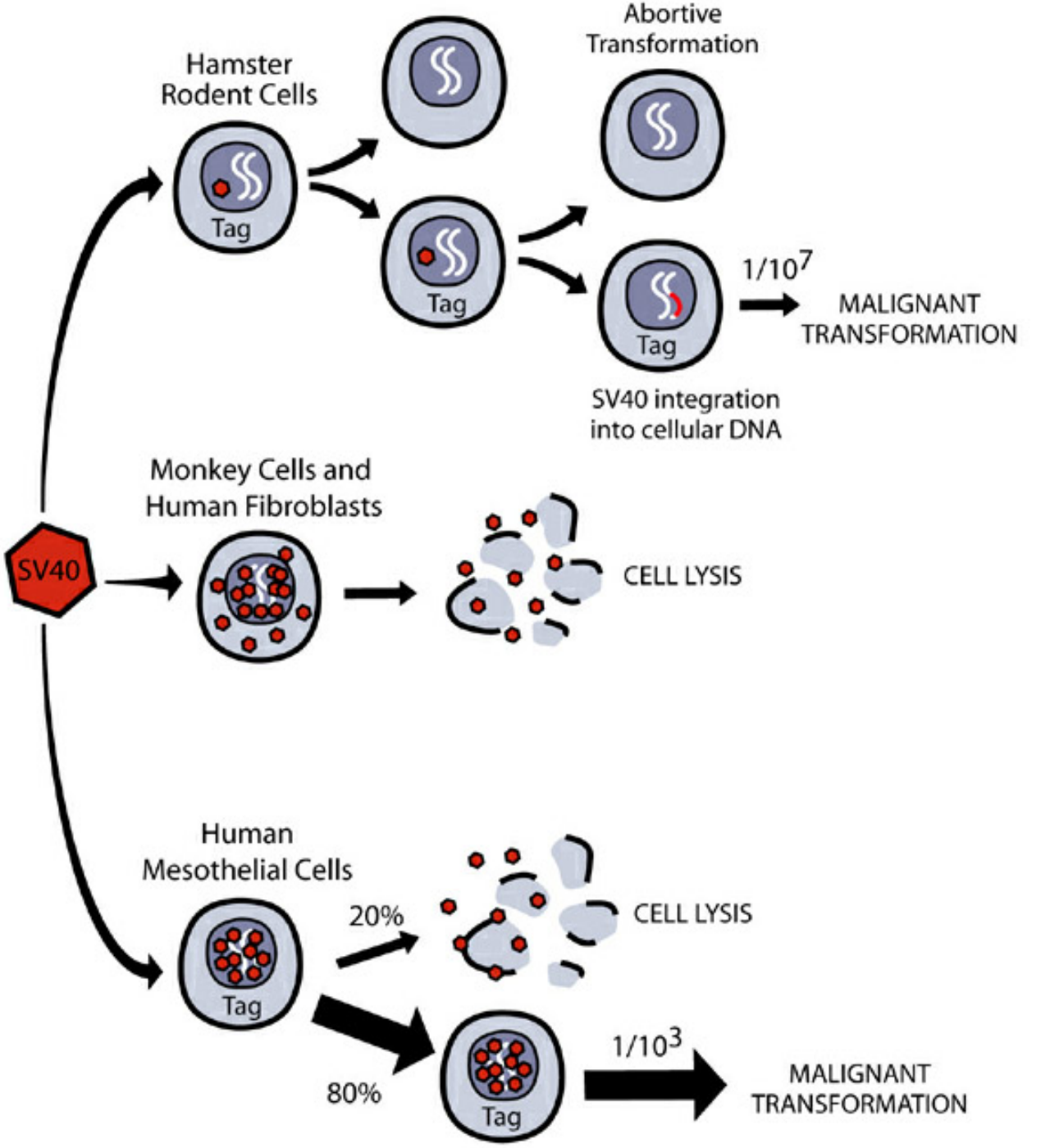
t
16

SV40 in human tumors

- More than 70 positive reports from 51 labs, IMIG and IARC. Five negative studies.
- Three international panels, one led by Dr. Klein Chair of the Nobel committee for Medicine, one by the NCI, and one by the IOM of the NAS-USA, all concluded that SV40 is present in some human MM and that SV40 is a strong transforming virus.

SV40 and Mesothelioma

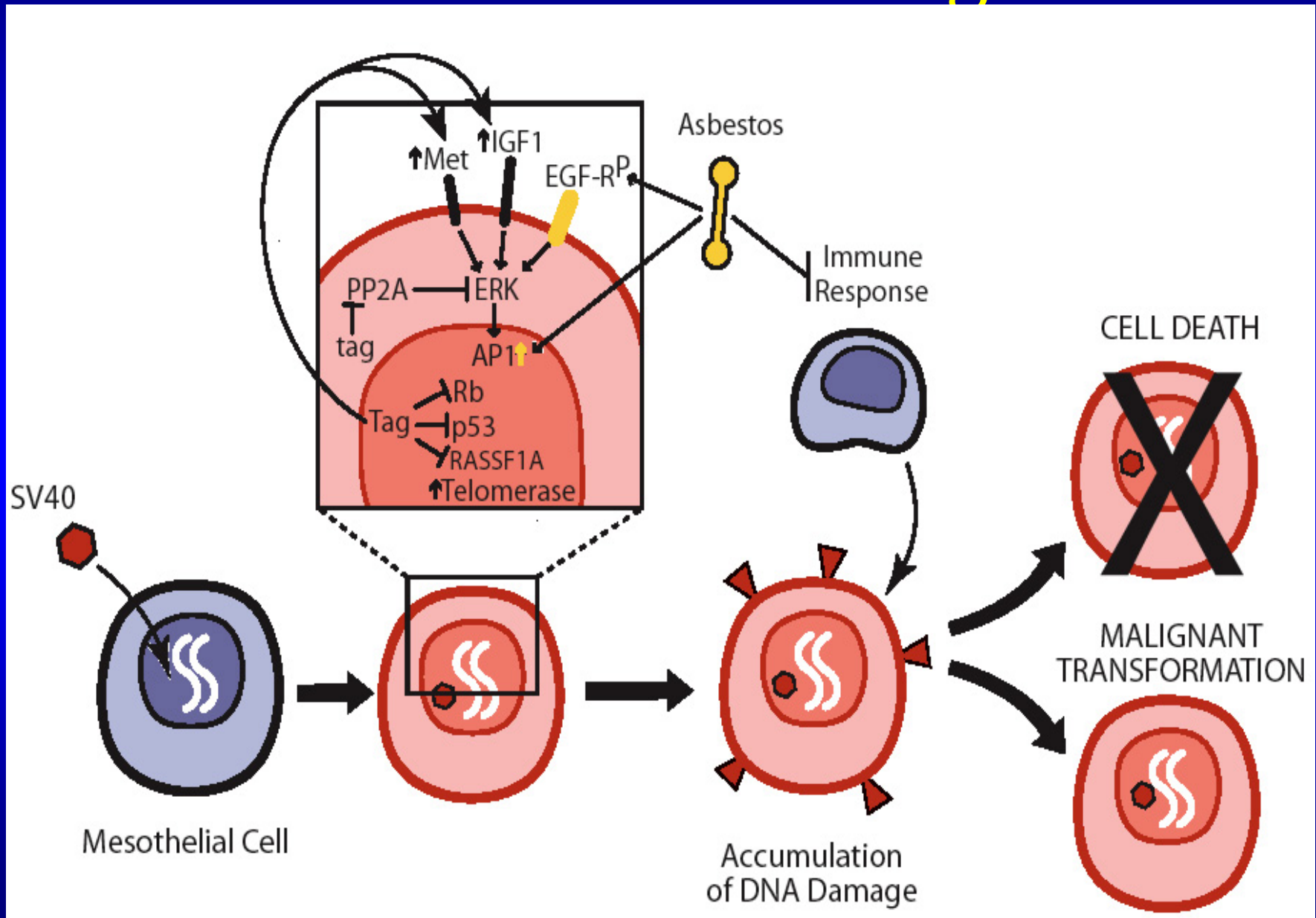
Is there a biological reason for the association of SV40 with mesothelioma?


Hamster
Rodent Cells
Tag
Abortive
Transformation
Tag
1/10^7
MALIGNANT
TRANSFORMATION
Tag
SV40 integration
into cellular DNA
Monkey Cells and
Human Fibroblasts
SV40
CELL LYSIS
Human
Mesothelial Cells
20%
CELL LYSIS
Tag
80%
1/10^3
MALIGNANT
TRANSFORMATION
Tag

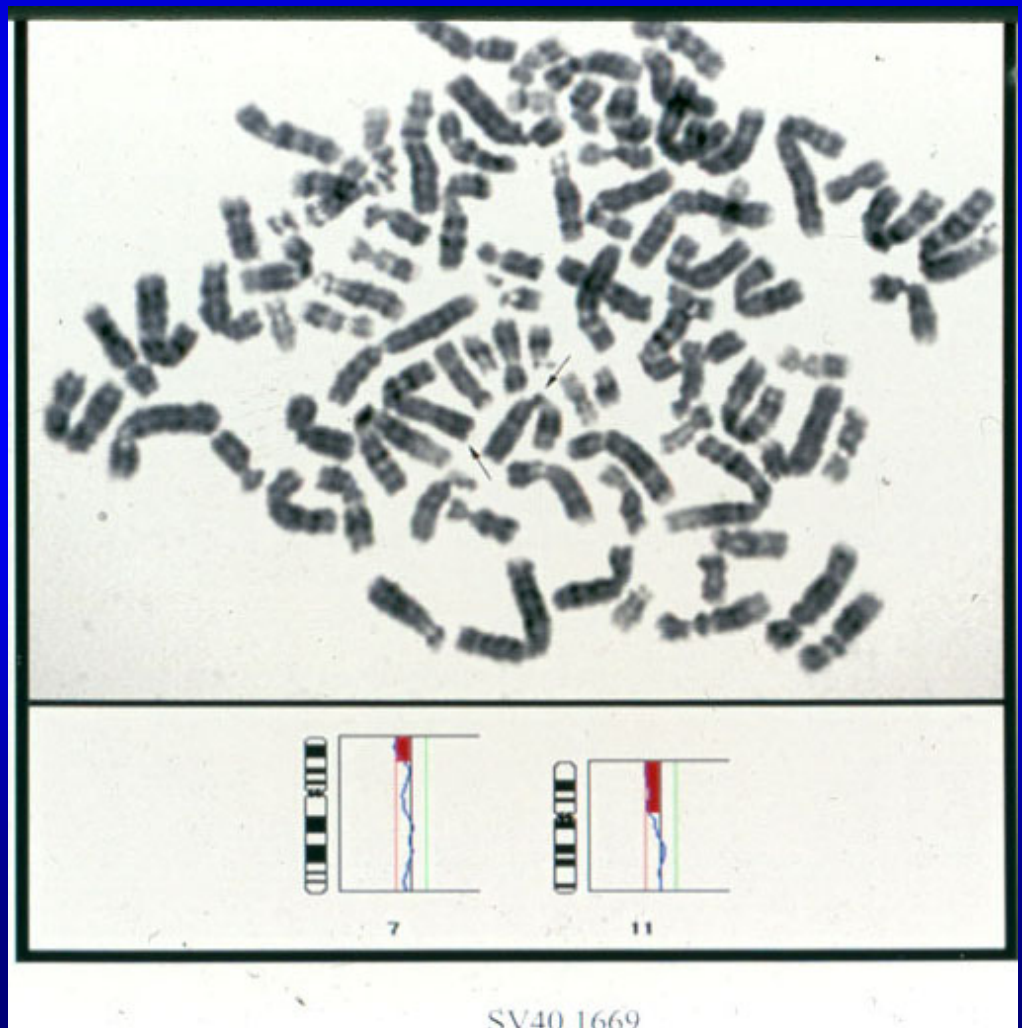
SV40 carcinogenesis

Mechanisms in mesothelioma

SV40-mediated carcinogenesis



SV40 genetic damage in humans. Cell with 85 chromosomes



Can SV40 cause human cancer?

- SV40-transformed human cells grew as subcutaneous tumors when injected into human volunteers.
  - Jensen et al., J. Natl. Cancer Inst.1964

Can SV40 cause human cancer?

- Yes, because SV40 is a potent human carcinogen
- However, viruses are seldom complete carcinogens and cancer development is not an inevitable outcome of virus infection in any viral system
- SV40 carcinogenesis must be studied together with the environmental and genetic factors associated with SV40+ tumors

From where is SV40 coming from?

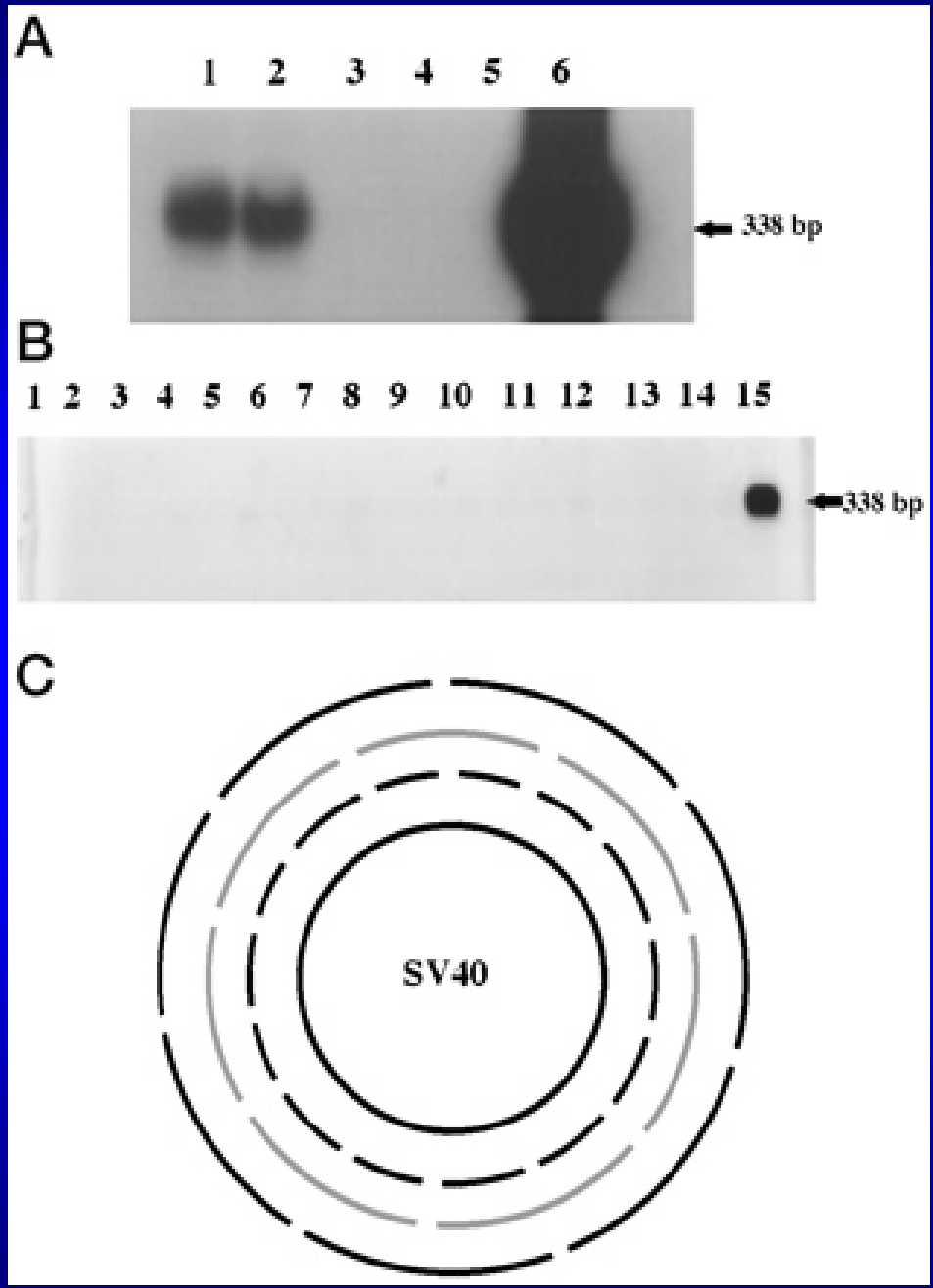
- ORIGIN OF SV40 IN HUMAN TUMORS:
  - CONTAMINATED VACCINES
  - DIRECT CONTACT WITH MONKEYS
  - LABORATORY PERSONNEL
  - HUMAN TO HUMAN TRANSMISSION?

From where is SV40 coming from?

- Several batches of Poliovaccines prepared in the US and in other countries were contaminated with infectious SV40 from 1954 until 1963
- The source of SV40 were both the original seed vaccines prepared by Salk, Sabin and others, and the monkeys used to propagate those vaccines in subsequent years

Poliovaccination in the US until September 1961

- < 1 year 2. 4 millions (55% of age group)
- 1-4 years 14.6 millions (87%)
- 5-9 years 18. 4 millions (93%)
- 10- 14 years 16. 9 millions (94%)
- 15-19 years 11.4 millions (84%)
- 20-39 years 26.3 millions (60%)
- 40-59 years 8.4 millions (19%)


A
1 2 3 4 5 6
338 bp
B
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
338 bp
C
SV40

Some SV40 found in humans comes from the poliovaccines

- In Cancer Res.1999 we published the presence of 2 unique strains of SV40 in poliovials prepared in 1954. Strain **MC028846B** and MC028863B
- **Three years later Butel's team found strain MC028846B in 3 lymphoma patients**: 42, 60 and 30 year old (HIV+)

Conclusions

- At least some of the SV40 found in human tumors originated from contaminated poliovaccines